NOT FOR PUBLICATION (Doc. No. 205)

**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

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| SCIELE PHARMA INC., (N/K/A SHIONOGI PHARMA INC.), ANDRX CORPORATION, ANDRX PHARMACEUTICALS, INC. (N/K/A WATSON LABORATORIES, INC., FLORIDA), ANDRX PHARMACEUTICALS, L.L.C., ANDRX LABORATORIES (NJ), INC. ANDRX EU LTD., and ANDRX LABS, L.L.C., | : | |
| Plaintiffs, | : | Civil No. 09-0037 (RBK/JS) |
| v. | : | |
| LUPIN LTD., and LUPIN PHARMACEUTICALS, INC., and MYLAN INC., and MYLAN PHARMACEUTICALS, INC. | : | |
| Defendants. | : | |

**KUGLER**, United States District Judge:

This matter comes before the Court on remand from the Federal Circuit's Order of February 6, 2012, which vacated this Court's December 6, 2011 Order and remanded for further findings of fact and conclusions of law. Sciele v. Lupin, No. 2012-1118 (Fed. Cir. Feb. 6, 2012) (order vacating this Court's preliminary injunction Order). The December 6, 2011 Order and accompanying Opinion ("Preliminary Injunction Opinion") granted the motion of Shionogi Pharma Inc. ("Plaintiff" or "Shionogi") for preliminary relief enjoining Lupin Ltd. and Lupin Pharmaceuticals, Inc. ("Defendant" or "Lupin") from importing a pharmaceutical product—a

generic version of Plaintiff's Fortamet®—into the United States, and/or selling that generic product.

The Federal Circuit has remanded the matter to this Court for findings of fact and conclusions of law specifically related to Lupin's argument that Shionogi's patent 6,866,866 (the "'866 Patent") is invalid on obviousness grounds, and that, therefore, Shionogi is not likely to succeed on the merits of its infringement. Specifically, we consider here whether Defendant's argument that prior art renders the '866 patent obvious, and therefore invalid, raises a substantial question that Plaintiff is not likely to succeed on the merits of its appeal and consequently is not entitled to the equitable relief of a preliminary injunction. In examining this question, we will not recite the factual history of this case, as we have done so on several other occasions. Instead, we incorporate by reference the factual summary included in both the Preliminary Injunction Opinion, Sciele Pharma, Inc. v. Lupin Ltd., 09-cv-37 D.I. 279, 2011 U.S. Dist. LEXIS 139892 (D. Del. Dec. 6, 2011), and this Court's Opinion following the claim construction hearing in this matter, Sciele Pharma, Inc. v. Lupin Ltd., 09-cv-37, 2011 U.S. Dist. LEXIS 105572 (D. Del. Sept. 15, 2011) ("Markman Opinion").

The Court determines that the findings of fact and conclusions of law articulated herein reiterate our December 6, 2011 finding that Lupin's obviousness argument does not raise a substantial question as to Shionogi's likelihood of success on the merits of its infringement claim. Incorporating this determination into the analysis of the four-pronged preliminary injunction inquiry undertaken in our Preliminary Injunction Opinion, the Court finds that the balance of preliminary injunction factors continues to weigh in Plaintiff's favor, and that injunctive relief is warranted in this case. That is, because Shionogi has shown a likelihood of success on the merits about which Lupin has not raised a substantial question (either through the

obviousness argument addressed here, or the other contentions considered in the Preliminary Injunction Opinion), because Shionogi has made the requisite showing that it will suffer irreparable harm in the absence of a preliminary injunction, because the balance of hardships tips in Shionogi's favor, and because the public policy considerations point equally in favor of Shionogi and Lupin, this Court finds that the preliminary injunction analysis weighs in Shionogi's favor. Therefore, the Court reissues the preliminary injunction according to those terms that existed before the Federal Circuit's remand.

## I. STANDARD FOR OBVIOUSNESS

In this case, Lupin argues that Shionogi is not likely to succeed on the merits of its claim for patent infringement because Lupin has presented a substantial question that Fortamet®'s '866 Patent is invalid for obviousness. 35 U.S.C. § 103(a) provides

> [a] patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

The United States Supreme Court has "set forth an expansive and flexible approach" to applying Section 103. KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 415 (2007). That four-step approach, elucidated in Graham v. John Deere Co. of Kansas City, indicates that "[u]nder § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." 383 U.S. 1, 17 (1966). Moreover, "objective evidence of nonobviousness" must also be considered. Takeda Chem. Indus. v. Alphapharm Pty., Ltd., 492 F.3d 1350, 1356 (citing KSR, 550 U.S. at 406; Graham, 383 U.S. at 17-18). The Graham test was further clarified in KSR v. Teleflex,

where the Court reiterated what it had held "for over half a century"—namely that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR, 550 U.S. at 415-16. KSR notably "acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.'" Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc., 655 F.3d 1291, 1304 (Fed. Cir. 2011) (quoting KSR, 550 U.S. at 418).

## II. FACTUAL FINDINGS

Plaintiff's drug, Fortamet®, is a hydrochloride tablet designed to provide for the extended-release of metformin to patients suffering from Type 2 diabetes mellitus. The '866 Patent is designed to extend the release of metformin so that its maximum concentration occurs at the time of night when the body's glucose production is highest. The '866 Patent thus teaches a mean time to maximum plasma concentration of 5.5 to 7.5 hours or 5.5 to 7.0 hours. See '866 Patent, claim 1 ("the dosage form provides a mean time to maximum plasma concentration ($T_{max}$) of the metformin from 5.5 to 7.5 hours after administration following dinner"); '866 Patent, claim 3 (claiming "[t]he controlled release oral dosage form of claim **1**, which provides a mean time to maximum plasma concentration ($T_{max}$) of metformin 5.5 to 7.0 hours after the administration of the dose").

Defendant argues that "all of the asserted claims of the '866 patent are presumptively invalid as obvious from Cheng (WO 99/47125), the foreign counterpart of '859, in view of Timmins (WO 99/47128)." Def. Br. in Opposition to Plaintiff's Motion for Preliminary Injunction (hereinafter, "Def. Br. Opp."), 20. Specifically, Defendant contends that the mean time to plasma concentration, or "$T_{max}$," established in the claims of the '866 Patent renders the

patent unobvious because it falls within the range patented by prior art (Timmins), and could be applied to prior art disclosing the remainder of the '866 Patent's claims (Cheng) by a person of ordinary skill in the art. Specifically, Lupin suggests that the Cheng patent is prior art that discloses every element of the '866 Patent except for the $T_{max}$ of 5.5 to 7.5 hours. Lupin further indicates that Timmins is prior art that discloses a $T_{max}$ of 4 to 8 hours. Therefore, Lupin's logic goes, because a person of ordinary skill in the art could modify Cheng to achieve the $T_{max}$ range claimed by the '866 Patent, the '866 Patent is obvious. Defendant's argument relies heavily on the Supreme Court's ruling in KSR.

The Court notes at the outset a fundamental factual difference between this case and KSR—namely, that in this case the prior art allegedly rendering the '866 Patent obvious was considered by the Patent and Trademark Office (PTO) when it approved the '866 Patent. In KSR, the Supreme Court highlighted the fact that the prior art that rendered obvious the patent in question was not before the PTO when the patent was under consideration. See KSR, 550 U.S. at 411 ("Engelgau had not included Asano among the prior art references, and Asano was not mentioned in the patent's prosecution. Thus, the PTO did not have before it an adjustable pedal with a fixed pivot point."). The '866 Patent challenged here contains explicit reference to both sources of prior art—Timmins and Cheng—upon which Defendant now rests its obviousness argument. See '866 Patent, 2:34-35 ("A controlled release metformin dosage form is also described in WO 99/47128 [Timmins]."); '866 Patent, 2:46-48 ("Our own WO 99/47125 [Cheng, '859 Patent] discloses controlled release metformin formulations providing a Tmax from 8 to 12 hours."). Moreover, Lupin has conceded that Timmins and Cheng were before the PTO when the '866 Patent was considered and approved. See Def. Br. Opp., 21. Thus, in contrast to

the situation in KSR, here the PTO had the opportunity to consider the prior art relevant to Lupin's obviousness defense.

Furthermore, the prosecution history of the '866 Patent explicitly reveals that the PTO not only had the opportunity to consider the prior art taught by Cheng, but in fact did consider it. A document entitled "Amendment Under 37 CFR § 1.111 and Statement of Substance of Interview Under 37 CFR § 1.133" describes a PTO interview on November 20, 2003, where a version of what later became the '866 Patent was discussed. The section entitled "Cheng et al" indicates that the PTO Examiner "considered the closest prior art to teach a $T_{max}$ of 8 hours (the Cheng, et al reference). The Examiner agreed that claim 5, which had an upper $T_{max}$ of 7.0 hours and which value is directly supported by the working examples, is patentably distinct over the Cheng, et al reference." Declaration of Former U.S. PTO Examiner Arthur J. Steiner ("Steiner Decl."), Def. Br. Opp., Ex. L, 9. Moreover, "[t]he Examiner further agreed to consider the patentability of the broader range to 7.5 hours [the $T_{max}$ value contained in claim 1 of the '866 Patent] if applicants were to provide a working example of that value, as well." Id.[1]

Timmins, which was before the PTO when the '866 Patent was approved, "relates to a new dosage form for highly water soluble medicaments, such as the antidiabetic metformin, . . . and to a method for preparing such dosage form." Declaration of Kenneth R. Morris, Ph.D. ("Morris Decl."), Def. Br. Opp., Ex. D, 1. Although Lupin represents that Timmins teaches the same $T_{max}$ as the '866 Patent, Timmins itself refers to a median $T_{max}$. This Court has defined "$T_{max}$" as translating to "mean time to plasma concentration," "the time period which elapses after administration of the dosage form at which the plasma concentration of the drug attains the highest plasma concentration of the drug attained within the dosing interval (i.e., about 24

[1] Indeed, as this Court explained in its Preliminary Injunction Opinion, the PTO did allow the $T_{max}$ of 7.5 hours, designated in claim 1, when it issued a Notice of Allowability of that claim in a "communication [that was] responsive to *interview conducted 11/20/03*." See Steiner Decl., Ex. I (emphasis in original).

hours)." Morris Decl., Ex. D, 34; Markman Op., 16. As Plaintiff's expert has explained, "[t]here is, in fact, no way to ascertain the mean $T_{max}$ value—or any mean value—given only the median and the range." Declaration of Lawrence L. Fleckenstein, Pharm.D. ("Fleckenstein Decl."), Pl. Br. in Support of Preliminary Injunction ("Pl. Br. Prelim. Inj."), at ¶ 83.

Moreover, Timmins indicates that "[t]he mean plasma profile demonstrated useful modification of drug release in vivo relative to the immediate release formulation and with no impact on bioavailability in contrast to other metformin extended release formulations reported in the literature." Morris Decl., Ex. D, 34. By contrast, the '866 Patent explains that "[i]t has surprisingly been found that when biguanides such as metformin are administered orally in a controlled release dosage form suitable for once-a-day dosing in the 'fed' state, . . . the bioavailability is improved . . . ." '866 8:53-56.

Having outlined the scope and content of the prior art, and the differences between the prior art and the claims at issue, we now consider the level of ordinary skill in the pertinent art. See Graham, 383 U.S. at 18. Defendant has argued that, during the prosecution of the '866 Patent, Plaintiff "made an admission that is devastating to their case now." Def. Br., 20. In a communication entitled "Amendment Under 37 C.F.R. § 1.111," Plaintiff informed the Examiner that "one skilled in the art would be able to manipulate the processes and formulations of the '859 [Cheng] by other methods to obtain the claimed pharmacokinetic parameters of the present invention by routine experimentation." Steiner Decl., Ex. E, 10. Plaintiff made this statement in its request to amend the application for what eventually became the '866 Patent, in response to the Office Action that rejected its previous patent application. Specifically, Plaintiff was responding to the Examiner's findings that "Applicant fails to set forth the criteria that defines the dosage form or steps in the production of the composition that results in the dosage form

having the instant claimed plasma profile," and that "Applicant fails to provide information allowing the skilled artisan to ascertain the plasma profile without undue experimentation." Id. at 7. The Court finds that Plaintiff's statement to the PTO does, indeed, indicate that a person of ordinary skill in the art could have manipulated Cheng to reach the '866 Patent's pharmokinetic parameters, allowing the prospective '866 Patent to meet the enablement requirement of 35 U.S.C. § 112. See Section III.C infra.

Finally, the Court evaluates the last prong of the Graham test—that objective evidence of nonobviousness must be considered—in light of evidence presented by Lupin. Lupin suggests that a study by the Bristol-Myers Squib Company ("BMS") that showed that BMS "was studying an extended release dosage form of metformin having a $T_{max}$ in the range of 4 to 8 hours would have motivated a person of skill in the art to try a formulation that had a $T_{max}$ in that range." Morris Decl. at ¶ 19. The Court notes that the BMS study was published in 2005, and the application for the '866 Patent was first filed on November 3, 2000 and was approved on March 15, 2005.

## III. LEGAL CONCLUSIONS

### A. Deference Due to a Qualified Government Agency

Lupin presents its obviousness argument in light of its view that the claims of the '866 Patent were not properly issued and, as a consequence, the '866 Patent is no longer entitled to a presumption of validity. See Def. Br. Opp., 21 ("Both the '859 patent (Cheng) and Timmins were admittedly references cited to the patent examiner, and ordinarily one would apply the presumption that the examiner must have found a patentable distinction between the issued claims and the cited prior art. But not here, because . . . the examiner did not ultimately allow the claims of the issued patent."). However, because this Court rejected Lupin's argument as to

the ‘866 Patent’s prosecution history, and found that all claims of the issued ‘866 Patent were, indeed, approved by the Patent and Trademark Office (“PTO”), the presumption of validity still applies. See Canon Computer Sys. v. Nu-Kote Int’l, 134 F.3d 1085, 1088 (Fed. Cir. 1998) (finding that, although “[i]t is true that [a plaintiff] carries the burden of establishing a likelihood of success on the validity issue and thus must show that [a defendant] will not likely prove that the patent is invalid[,]” nevertheless “a patent is presumed valid, and this presumption exists at every stage of the litigation”).

As the Federal Circuit has found, “where the challenger fails to identify any persuasive evidence of invalidity, the very existence of the patent satisfies the patentee’s burden on the validity issue.” Id. This is because, as the Federal Circuit has also made clear, “[w]hen the party asserting invalidity relies on references that were considered during examination or reexamination,” as is the case with the ‘866 Patent, “that party [i.e., Lupin] bears the added burden of overcoming the deference that is due to a qualified government agency presumed to have done its job.” Pharmastem Therapeutics, Inc. v. Viacell, Inc., 491 F.3d 1342, 1366 (Fed. Cir. 2007) (internal quotation omitted). For the reasons expressed in Section III.A.2 of our Preliminary Injunction Opinion, this Court finds that deference to a qualified government agency—the PTO—is owed here, and that, as a result, the ‘866 Patent is presumed valid.

**B. KSR v. Teleflex Analysis**

Defendant argues that the Supreme Court’s ruling in KSR v. Teleflex necessitates a finding that Plaintiff is unlikely to succeed on the merits of its claim because its ‘866 Patent is invalid for obviousness. KSR reiterated the Supreme Court’s finding that a “‘patent for a combination which only unites old elements with no change in their respective functions . . . obviously withdraws what already is known into the field of its monopoly and diminishes the

resources available to skillful men,'" thus offering "a principal reason for declining to allow patents for what is obvious." KSR, 550 U.S. at 415-16 (quoting Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152-53 (1950)). Thus Lupin raises the question of whether the modification of Cheng in light of Timmins is a modification that would have been obvious to one of ordinary skill in the art.

First, as indicated in Section II supra, this case differs sharply from KSR because the prior art that, according to Lupin, renders the '866 Patent invalid for obviousness was before the PTO when the '866 Patent was issued. In KSR, the Supreme Court pointed out that the prior art in question was not before the PTO when the patent was approved. 550 U.S. at 411. Moreover, the Teleflex district court, whose reasoning the Supreme Court later affirmed in KSR, "[found] persuasive Defendant's argument that if Asano had been cited to the Examiner, he would have found the combination of Asano and Smith to be obvious, just as he found the combination of Redding and Smith to be obvious." Teleflex Inc. v. KSR Int'l Co., 298 F. Supp. 2d 581, 595 (E.D. Mich. 2003). In the instant case, Timmins and Cheng were both cited to the Examiner, and the Examiner did not find it obvious to use them together in the '866 Patent.

Furthermore, the Court notes that, as explained above, the $T_{max}$ of 5 hours taught in Timmins represents a median value, as opposed to the mean $T_{max}$ of 5.5 to 7.5 hours specified in the '866 Patent. Therefore, it cannot be said that the '866 Patent "only unites" Timmins and Cheng "with no change in their respective functions," since the teaching of Timmins that, Lupin argues, was mobilized by Cheng, is not precisely the art that Timmins taught. Moreover, as Shionogi pointed out in its brief to the Federal Circuit, Timmins did not teach increased bioavailability, making its addition to Cheng—which did teach increased bioavailability—nonobvious. Pl. Br. to Fed. Cir., 38-39.

Moreover, the Court finds unavailing Lupin's argument that the BMS study proves the obviousness of the '866 patent. Given that the '866 patentees had been motivated to achieve the $T_{max}$ sought in the BMS study five years before the study was published, Lupin's argument that the BMS study "would have motivated" a person of skill in the art to achieve the $T_{max}$ achieved by the '866 Patent is unpersuasive. Given this, and in light of the factual findings noted above—particularly the deference owed to the PTO's assessment of the prior art before it—the Court finds that the BMS study is not sufficient to raise a substantial question of obviousness.

**C. Enablement v. Obviousness**

As to Plaintiff's statement to the PTO that one of ordinary skill in the art would be able to manipulate other controlled-release technologies to achieve the $T_{max}$ specified in the '866 Patent, the Court finds, contrary to Defendant's argument, that this "admission" is hardly "devastating" to the validity of Plaintiff's patent. Plaintiff's statement was made to satisfy the enablement requirement of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As the Federal Circuit has explained, "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988). Plaintiff's statement that a person of ordinary skill in the art would be able to produce the claimed $T_{max}$ simply expresses that the Federal Circuit's test of enablement has been satisfied. To interpret Plaintiff's statement as Lupin does would be to suggest that a patent's ability to satisfy the enablement requirement of Section 112 would always

provide evidence of invalidity for obviousness under Section 103(a)—a result that this Court finds difficult to approve.

## IV. CONCLUSION

This Court concludes that, particularly in light of the high burden of proof created by the necessary deference to the PTO, Lupin's obviousness argument does not raise a substantial question as to the validity of the '866 Patent, and therefore has not raised a substantial question as to Shionogi's likelihood of success on the merits of its patent infringement case. Accordingly, this Court's analysis of the preliminary injunction factors is reinforced—not disturbed—by our analysis of Lupin's obviousness contentions, and this Court again finds that balance of the four factors weighs in favor of granting Shionogi's motion for a preliminary injunction.

Therefore, for the foregoing reasons, and for the reasons stated in this Court's Preliminary Injunction Opinion, Plaintiff's motion for preliminary injunction is **GRANTED**. The sum of $15,000,000 posted by Plaintiff on December 12, 2011, pursuant to Federal Rule of Civil Procedure 65(c) and this Court's Order, will remain posted as security pursuant to Rule 65(c).

Dated: 2/14/2012

/s/ Robert B. Kugler
ROBERT B. KUGLER
United States District Judge